

REMARKS

Attached hereto is a marked-up version of the changes made to the claims by the above amendment. The attached page is captioned **“Version with markings to show changes made.”**

Support for the amendments to claims 21 and 32 are found at least in claim 22 as previously presented. The production of micelles is described in detail in the instant specification, especially on pages 38-48.

Claim 27 has been amended to be consistent with claim 21.

Claim 28 has been amended to recite “butylated hydroxytoluene” and “ascorbyl palmitate” as supported by page 32 of the specification.

Claim 33 has been amended to recite “benzoporphyrin derivative monoacid ring A (BPD-MA)” in place of “verteporfin”. Support for the amendment is provided at least on page 25-26 of the specification.

Claim 37 has been canceled as a duplication of claim 32.

The subject matter of claim 38 has been combined into claim 39, and claim 40 has been canceled, without acquiescence to any position set forth in the Office Action. Applicants reserve the right to pursue the subject matter of claims 38 and 40 in a continuing application. Claim 39 has also been amended to correct a clerical error and to be consistent with claim 32, from which it depends.

The amendment to claims 21 and 32 to recite “micelles” has been made for reasons related to business considerations and commercially contemplated embodiments of the invention rather than in acquiescence to any position set forth in the Office Action. Applicants reserve the right to pursue the claim as originally filed in a continuing application.

No new matter has been introduced, and entry of the amendments is respectfully requested.

Rejections under 35 U.S.C. § 112

Claims 21-40 have been rejected under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter not described in the specification and thus containing new matter. Applicants have carefully reviewed the statement of the rejection and believe that it is based on

the view that the negative limitations concerning “egg phosphatidylglycerol” in claims 21, 30 and 40, “egg phospholipid” in claim 30, and “verteporfin” in claim 33 do not have support in the application as filed. Applicants traverse for the following reasons.

As an initial matter, Applicants point out that claim 33 has been amended to recite benzoporphyrin derivative monoacid ring A (BPD-MA) in place of “verteporfin” as described above. Additionally, claim 40 has been canceled with reservation of the right to pursue it in a continuing application.

Additionally, Applicants respectfully point out that the specification on page 28, second paragraph, describes the use of unsaturated phosphatidylglycerols as a whole in the practice of the invention and then describes the possible use of egg phosphatidylglycerol (EPG) as a one possibility. Stated differently, the specification discloses the whole of unsaturated phosphatidylglycerols as a genus and then details a number of species, including EPG, within the genus. Applicants respectfully submit that the setting out of the whole along with the specific species of EPG necessarily means that the part remaining as the whole with the exclusion of EPG. This is consistent with the discussion in *In re Johnson*, 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977) as quoted at MPEP 2173.05(i): “[the] specification, having described the whole, necessarily described the part remaining.”

Applicants therefore respectfully submit that no new matter exists with regard to the concept of “unsaturated phosphatidylglycerols is not egg phosphatidylglycerol” as recited in claims 21 and 32.

In a similar manner, the specification on page 28, first paragraph, describes the use of phospholipids as a whole in the practice of the invention and then describes the possible use of “egg or soybean phospholipid”. Once again, the specification discloses the whole of phospholipids as a genus and then details a number of species, including egg phospholipid, within the genus. Therefore, and in accordance with the standard set forth in *In re Johnson* and at MPEP 2173.05(i), Applicants respectfully submit that no new matter exists with regard to the concept of “phospholipids ... do not comprise egg phospholipid” as recited in claim 30.

Last, Applicants point out that the specification on pages 7-8, bridging paragraph, describes the use of “hydrophobic agents” in the practice of the invention. This description continues on page 8 to describe the possible use of photosensitizers and benzoporphyrin derivative monoacid ring A (BPD-MA), which is also discussed on pages 25-26. As explained

above, because the specification discloses the whole of “hydrophobic agents” as a genus and then details species such as BPD-MA, Applicants respectfully submit that no new matter exists with regard to the concept of “one or more hydrophobic agent is one or more photosensitizer but does not comprise benzoporphyrin derivative monoacid ring A (BPD-MA)” as now recited in claim 33.

In light of the above discussion, Applicants respectfully submit that no issue of new matter is encompassed by the language of the claims, and this rejection may be properly withdrawn.

Claims 23, 28, 31, 34, 38 and 39 have been rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite. Applicants have carefully reviewed the statement of the rejection which appears based on a requirement for full chemical names for photosensitizers and the term “high” recited in the claims. Applicants believe that the claims are definite and traverse for the following reasons.

Claim 23 has been amended to recite “benzoporphyrin derivative monoacid ring A (BPD-MA)” where appropriate. The terms “A-EA6” and “B-EA6” are the identifiers for the photosensitizers as represented on page 27 of the application. They are not abbreviations or acronyms that may be spelled out in their entireties. Applicants believe these identifiers raise no issue of indefiniteness in light of page 27, and no introduction of the formulas from page 27 into the claims is necessary. Therefore claims 23, 31 and 34 are definite as presented.

Claim 28 has been amended to recite “butylated hydroxytoluene” and “ascorbyl palmitate” as supported by page 32 of the specification.

Contrary to the instant statement of rejection, claims 38 and 39 recite “high energy manipulation”, which is analogous to “high energy manipulation” as a term describing a class of processes disclosed in the specification and known in the art. The word “high” is not used in a relative sense and so no issue of indefiniteness exists with respect to the use of the word. To advance prosecution and without acquiescence to the instant rejection, however, the subject matter of claims 38 and 39 have been combined into amended claim 39 without use of the term.

Applicants respectfully submit that the above addresses all issues raised with respect to the instant rejection, which may now be properly withdrawn withdrawn.

Prior art rejection under 35 U.S.C. § 102(b)

Claims 21-25, 29, 32, 33 and 38-40 have been rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Madden (USP 5,389,378). Applicants have carefully reviewed the statement of the rejection and the cited prior art and traverse for the following reasons.

Claims 21 and 32 have been amended to relate to micelles and methods for their production. Madden fails to teach, suggest or otherwise indicate a composition comprising micelles or the production thereof as now claimed. The term “micelle” or variations thereof, is not even used in the Madden patent.

Accordingly, Madden fails to anticipate claims 21, 23-25, 29, 32, 33 and 39 as amended (with claims 22, 38 and 40 having been canceled), and withdrawal of the instant rejection is respectfully requested.

Claims 21-24, 27-29, 32, 33, 35, 36, and 38-40 have been rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Liu (USP 5,707,608) or Desai et al. (USP 6,074,666). Applicants have carefully reviewed the statement of the rejection and the cited prior art and traverse for the following reasons, which address each reference in turn.

As with Madden above, Liu fails to teach, suggest or otherwise indicate a composition comprising micelles or the production thereof as now recited in claims 21 and 32. The term “micelle” or variations thereof, are not even used in the Liu patent except in a single instance referring to how certain photosensitizers are *not soluble* in micellar solutions (see column 7, lines 32-39). Liu’s teachings are directed to liposomes and their production rather than to micelles.

Accordingly, Liu fails to anticipate claims 21, 23, 24, 27-29, 32, 33, 35, 36 and 39 as amended (with claims 22, 38 and 40 having been canceled).

With respect to Desai et al., Applicants also note that like Madden, Desai et al. fail to use the term “micelle” or variations thereof. This follows because the disclosure by Desai et al. relates to liposomes and their production rather than micelles. Accordingly, Desai et al. also fails to anticipate claims 21, 23, 24, 27-29, 32, 33, 35, 36 and 39 as amended.

In light of the above discussion, withdrawal of the instant rejection in its entirety is respectfully requested.

Prior art rejection under 35 U.S.C. § 103

Claims 25-30, 32 and 35-37 have been rejected under 35 U.S.C. § 103(a) as unpatentable over Madden (cited above). Applicants have carefully reviewed the statement of the rejection as well as the cited references respectfully traverse as follows.

As noted in the instant specification, the invention resides in part upon the unexpected discovery that micelles would be formed from bilayer (liposome) forming lipids by use of a high energy process such as microfluidization (see page 6, first paragraph). Madden completely fails to teach, suggest, or otherwise indicate the production of micelles. That is why the instant claims are directed to a discovery that is unexpected over Madden.

Contrary to statements on page 6 of the Action concerning the teachings of Madden, he *does not* teach the use of a high energy processing step that would produce micelles. As an initial matter, Madden does not use the terms “high energy process”, “microfluidization”, “sonication”, “high speed shearing”, “homogenization” or variants thereof. Beginning in column 6, line 36, Madden describes the use of extrusion to size liposomes. As noted on page 43, lines 3-5 of the instant specification, however, *extrusion does not produce micelles*. This is consistent with the fact that Madden does not disclose or suggest the production of micelles.

Therefore, there is no means by which Madden’s disclosure, even if it recites the use of the same liposome forming phospholipids as recited in the instant claims, will motivate the artisan of ordinary skill to produce micelles. There wasn’t any expectation of producing micelles, much less a reasonable expectation of success in producing them. Accordingly, claims 25-30, 32, 35 and 36 (with claim 37 having been canceled) are patentable over Madden.

Additionally, and with respect to claim 36, pages 44-45 of the instant specification describe how the use of a temperature below 30°C favors the production of micelles, which are smaller than liposomes. The top of page 45 also describes how the use of lower temperature is actually expected in the art to result in the production of larger particles. Therefore, and with respect to the assertion in the statement of the instant rejection, any allegation that it would have been obvious to the artisan of ordinary skill to use a temperature below 30°C is overcome by the unexpected discovery that it unexpectedly produces smaller particles in the form of micelles.

In light of the above discussion, Applicants respectfully submit that the instant rejection may be properly withdrawn.

Claims 25, 26, 30 and 40 have been rejected under 35 U.S.C. § 103(a) as unpatentable over Liu or Desai et al. (both as cited above). Applicants have carefully reviewed the statement of the rejection as well as the cited references and understand the rejection to be based upon either one of the two references in the alternative and not in combination. Applicants respectfully traverse as follows, which addresses each cited reference in turn.

As discussed on the previous page with respect to Madden, the invention is based in part on an unexpected discovery of micelle formation with bilayer (liposome) forming phospholipids. Liu completely fails to teach, suggest, or otherwise indicate the production of micelles. Therefore, the instantly claimed invention is directed to an unexpected discovery over Liu.

Furthermore, there is no means by which Liu's disclosure, even if it recites the use of the same liposome forming phospholipids as recited in claims 25, 26, and 30 (claim 40 having been canceled), will motivate the artisan of ordinary skill to produce micelles. Again, no expectation of producing micelles was present. Accordingly, claims 25, 26 and 30 are patentable over Liu.

Similarly, Desai et al. also completely fail to teach, suggest, or otherwise indicate the production of micelles. Therefore, instant claims 25, 26 and 30 are directed to an unexpected discovery over Liu. Once again, even if Desai et al. recites the use of the same liposome forming phospholipids as recited in claims 25, 26, and 30 the artisan of ordinary skill would have no motivation to, and no expectation of success in, producing micelles.

In light of the above, claims 25, 26 and 30 are patentable over Liu or Desai et al. individually, and even in combination. Applicants therefore, respectfully request that this rejection be withdrawn.

Claims 22, 23, 31, 34 and 37 have been rejected under 35 U.S.C. § 103(a) as unpatentable over Madden, Liu or Desai et al. (all as cited above). Applicants have carefully reviewed the statement of the rejection as well as the cited references and are uncertain whether the instant rejection is based upon the references individually or in some combination. Clarification is respectfully requested.

Nevertheless, Applicants review indicates that the references, individually or in combination, fail to render the claims obvious and so respectfully traverse as follows.

Claims 23, 31, and 34 (with claims 22 and 37 having been canceled) are directed to micelles comprising particular photosensitizers. While the statement of the rejection alleges that

the “high energy processing steps” of the references would result in the formation of micelles, Applicants again note that *the extrusion process of Madden would not produce micelles* and that none of the cited references describe the production of micelles. There is no *prima facie* case presented that any micelles were produced, or even expected, by the methods of any of the cited references, alone or in combination.

In light of these deficiencies in the cited references, it cannot be obvious that use of the photosensitizers recited in any of claims 23, 31, or 34 in the methods of the cited references, alone or in combination can result in the claimed compositions or methods. Therefore, no *prima facie* case of obviousness exists, and this rejection should be withdrawn.

Conclusion

Applicants believe that the claims are in condition for allowance and urge early indication to that effect. The Examiner is encouraged to contact the undersigned to expedite prosecution of the instant application.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 273012011300.

Respectfully submitted,

Dated: October 17, 2002

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

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JAN 24 2003

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In the Claims:

Kindly amend the claims as follows:

21. (amended) A composition comprising [~~microaggregates~~] micelles, said [~~microaggregates~~] micelles comprising saturated and unsaturated phospholipids and one or more hydro-monobenzo-porphyrin photosensitizer wherein said unsaturated phospholipid is not egg phosphatidylglycerol.

27. (amended) The composition of claim 21 wherein said [~~microaggregates~~] micelles further comprise at least one antioxidant.

28. (amended) The composition of claim 27 wherein said at least one antioxidant is butylated hydroxytoluene (BHT) and/or ascorbyl palmitate (AP).

32. (amended) A method for making a composition of [~~microaggregates~~] micelles comprising
producing a mixture of an organic solvent, a hydrophobic agent and saturated and unsaturated phospholipids to form an "intermediate complex";
removing said solvent to produce a "presome" material,
hydrating said "presome" material with an aqueous solvent, and
processing said hydrated material to produce [~~microaggregates~~] micelles,
wherein said unsaturated phospholipid is not egg phosphatidylglycerol.

33. (amended) The method of claim 32 wherein said one or more hydrophobic agent is one or more photosensitizer but does not comprise [~~Verteporfin~~] benzoporphylin derivative monoacid ring A (BPD-MA).

39. (amended) The method of claim [38] 32 wherein said [~~high-energy manipulation~~] processing step is selected from the group consisting of microfluidization, sonication, high speed shearing, [~~extrusion, sonication~~] and homogenization.